

## Refine Search

### Search Results -

Terms	Documents
sh2 adj containing adj inositol adj phosphatase\$	5

**Database:**  US Pre-Grant Publication Full-Text Database  
 US Patents Full-Text Database  
 US OCR Full-Text Database  
 EPO Abstracts Database  
 JPO Abstracts Database  
 Derwent World Patents Index  
 IBM Technical Disclosure Bulletins

**Search:** L1

### Search History

DATE: Wednesday, February 04, 2004 [Printable Copy](#) [Create Case](#)

Set Name Query  
side by side

Hit Count Set Name  
result set

DB=USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=NO; OP=OR

L1 sh2 adj containing adj inositol adj phosphatase\$ 5 L1

END OF SEARCH HISTORY

## Refine Search

### Search Results -

Terms	Documents
ship same inhibit\$ and (allograft or rejection)	12

**Database:**

US Pre-Grant Publication Full-Text Database  
US Patents Full-Text Database  
US OCR Full-Text Database  
EPO Abstracts Database  
JPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

**Search:**

L2

Refine Search

Recall Text      Clear      Interrupt

### Search History

**DATE:** Wednesday, February 04, 2004 [Printable Copy](#) [Create Case](#)

**Set Name Query**  
side by side

**Hit Count Set Name**  
result set

*DB=USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=NO; OP=OR*

<u>L2</u>	ship same inhibit\$ and (allograft or rejection)	12	<u>L2</u>
<u>L1</u>	ship same inhibit\$ same (allograft or rejection)	1	<u>L1</u>

END OF SEARCH HISTORY

?s ship (s) (inhibit?) and (allograft or reject?)  
Processing  
Processed 10 of 37 files ...  
Completed processing all files  
    118692 SHIP  
    7117567 INHIBIT?  
        1187 SHIP(S) INHIBIT?  
    148341 ALLOGRAFT  
    442663 REJECT?  
S1       13 SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)  
?rd  
...completed examining records  
    S2       4 RD (unique items)  
?show files;ds;t/3,k/all  
File 5:Biosis Previews(R) 1969-2004/Feb W1  
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    (c) 2004 NTIS, Intl Cpyrght All Rights Res  
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    (c) format only 2004 The Dialog Corp.  
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    (c) 2004 Elsevier Science B.V.  
File 266:FEDRIP 2004/Dec  
    Comp & dist by NTIS, Intl Copyright All Rights Res  
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    (c) 2004 DECHEMA  
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    (c) 2004 Thomson Derwent & ISI  
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    (c) 2004 Reed Business Information Ltd.  
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    (c) 2004 CAB International  
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    (c) 2004 Contains copyrighted material  
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(c) 2004 Mass. Med. Soc.  
File 467:ExtraMED(tm) 2000/Dec  
(c) 2001 Informania Ltd.

Set        Items      Description  
S1            13     SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)  
S2            4      RD (unique items)  
>>>KWIC option is not available in file(s): 399

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Set Items Description
-----
?s ship (s) (inhibit?) and (allograft or reject?)
Processing
Processed 10 of 37 files ...
Completed processing all files
    118692 SHIP
    7117567 INHIBIT?
    1187 SHIP(S) INHIBIT?
    148341 ALLOGRAFT
    442663 REJECT?
S1      13 SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)
?rd
...completed examining records
    S2      4 RD (unique items)
?show files;ds;t/3,k/all
File   5:Biosis Previews(R) 1969-2004/Feb W1
        (c) 2004 BIOSIS
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Set Items Description  
S1 13 SHIP (S) (INHIBIT?) AND (ALLOGRAFT OR REJECT?)  
S2 4 RD (unique items)  
>>>KWIC option is not available in file(s): 399

2/3,K/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2004 BIOSIS. All rts. reserv.

0013639526 BIOSIS NO.: 200200233037  
**Influence of SHIP on the NK repertoire and allogeneic bone marrow transplantation**  
AUTHOR: Wang Jia-Wang; Howson Julie M; Ghansah Tomar; Desponts Caroline;  
Ninos John M; May Sarah L; Nguyen Kim H T; Toyama-Sorimachi Noriko; Kerr  
William G (Reprint)  
AUTHOR ADDRESS: Immunology Program, Departments of Interdisciplinary  
Oncology and Biochemistry, H. Lee Moffitt Comprehensive Cancer Center and  
Research Institute, University of South Florida, Tampa, FL, 33612, USA\*\*  
USA  
JOURNAL: Science (Washington D C) 295 (5562): p2094-2097 15 March, 2002  
2002  
MEDIUM: print  
ISSN: 0036-8075  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

...ABSTRACT: major histocompatibility complex (MHC) class I influence  
engraftment and graft-versus-tumor effects after allogeneic bone marrow  
transplantation. We find that SH2-containing inositol phosphatase (\*SHIP\*  
) influences the repertoire of NK receptors. In adult \*SHIP\*-/- mice, the  
NK compartment is dominated by cells that express two \*inhibitory\*  
receptors capable of binding either self or allogeneic MHC ligands. This  
promiscuous repertoire has significant functional consequences, because  
\*SHIP\*-/- mice fail to \*reject\* fully mismatched allogeneic marrow grafts  
and show enhanced survival after such transplants. Thus, \*SHIP\* plays an  
important role in two processes that limit the success of allogeneic  
marrow transplantation: graft \*rejection\* and graft-versus-host disease.

DESCRIPTORS:

DISEASES: graft \*rejection--

MESH TERMS: Graft \*Rejection\* (MeSH...)

2/3,K/2 (Item 1 from file: 266)  
DIALOG(R)File 266:FEDRIP  
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00356977

IDENTIFYING NO.: 5R01HL72523-02 AGENCY CODE: CRISP

**Role of SHIP in Control of NK Cell Function**

PRINCIPAL INVESTIGATOR: KERR, WILLIAM G

ADDRESS: KERRW@MOFFITT.USF.EDU UNIVERSITY OF SOUTH FLORIDA 12902 MAGNOLIA DR-IMMUN PROGRAM

PERFORMING ORG.: UNIVERSITY OF SOUTH FLORIDA, TAMPA, FLORIDA

SPONSORING ORG.: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

DATES: 2007/01/02 TO 2006/30/06 FY : 2003

SUMMARY: DESCRIPTION (provided by the applicant): We find that the SH2-containing Inositol Phosphatase (\*SHIP\*) plays a crucial role in defining the \*inhibitory\* repertoire of NK cells in vivo. Four key findings made by our group support this hypothesis: (1) \*SHIP\* is recruited to both Ly49A and Ly49C in vivo, (2) the 85kD regulatory subunit of P1-3-Kinase (P13K) is recruited to Ly49A in vivo, (3) Akt is constitutively active in \*SHIP\*-/- NK cells in vivo and (4) a subset of NK cells that co express Ly49A and Ly49C dominates the adult NK compartment in \*SHIP\*-/- mice. Ly49A and Ly49C can interact with self MHC ligands in our \*SHIP\*-/- mice, but also ligands of other MHC haplotypes. This promiscuous NK \*inhibitory\* repertoire has profound functional consequences as \*SHIP\*-/- mice fail to \*reject\* fully histo-incompatible marrow grafts. Strikingly, we find that survival of \*SHIP\*-/- mice is dramatically enhanced relative to wild-type littermates following transplantation of fully histo-incompatible marrow. These findings demonstrate a critical role for \*SHIP\* in two processes that limit the success of histo-incompatible marrow transplantation: graft \*rejection\* and graft-vs.-host disease. We now propose to confirm and extend our initial observations to gain a better understanding of how \*SHIP\* shapes the NK cell \*inhibitory\* repertoire and to better understand how this impacts marrow transplantation across major histocompatibility barriers. Specifically we will: (1) Determine the mechanism by which \*SHIP\* influences the NK \*inhibitory\* repertoire, (2) Determine whether a "self-restricted" NK \*inhibitory\* repertoire alters the ability of NK cells to respond to activating receptors and (3) Determine the mechanism for failure of graft \*rejection\* and abrogated GVHD during allogeneic BMT in SH1P-/- mice.

DESCRIPTORS: laboratory mouse; bone marrow transplantation; natural killer cell; leukocyte activation /transformation; phosphomonoesterase; inositol; graft versus host disease; transplantation immunology; enzyme activity; transplant \*rejection\*

2/3,K/3 (Item 1 from file: 357)  
DIALOG(R)File 357:Derwent Biotech Res.  
(c) 2004 Thomson Derwent & ISI. All rts. reserv.

0293601 DBR Accession No.: 2002-15448 PATENT

Suppressing or preventing \*rejection\* of transplant in patient, or treating or preventing graft-versus-host disease in patient comprises administration of a substance that inhibits SH2-containing inositol polyphosphatase function - vector mediated gene transfer and expression in host cell for transplantation therapy, drug screening and gene therapy

AUTHOR: KERR W G

PATENT ASSIGNEE: UNIV SOUTH FLORIDA 2002

PATENT NUMBER: WO 200224233 PATENT DATE: 20020328 WPI ACCESSION NO.: 2002-435045 (200246)

PRIORITY APPLIC. NO.: US 314099 APPLIC. DATE: 20010823

NATIONAL APPLIC. NO.: WO 2001US29158 APPLIC. DATE: 20010919

LANGUAGE: English

Suppressing or preventing \*rejection\* of transplant in patient, or treating or preventing graft-versus-host disease in patient comprises

administration of a substance that inhibits SH2-containing inositol polyphosphatase...

**ABSTRACT:** DERTWENT ABSTRACT: NOVELTY - Suppressing or preventing \*rejection\* of transplant in a patient, or treating or preventing graft-versus-host disease (GVHD) in a patient having or in need of a transplant, by administering to the patient, a substance (I) that \*inhibits\* SH2-containing inositol polyphosphatase (\*SHIP\*) function. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a therapeutic composition comprising a substance that \*inhibits\* \*SHIP\* function in a carrier; (2) screening (M1) a substance suspected of \*inhibiting\* \*SHIP\* function involves providing a cell line that comprises an indicator of \*SHIP\* function; contacting the cell line with the substance; and measuring the response of the indicator to the substance, where the effectiveness of the substance as an \*inhibitor\* of \*SHIP\* function is assessed from the response to the indicator; (3) screening a candidate genetic construct for \*inhibiting\* \*SHIP\* function, involves providing an NK cell line that comprises an indicator of \*SHIP\* function, contacting the cell line with the genetic construct; and measuring the response of the indicator to the genetic construct; whereby the effectiveness of the genetic construct as an \*inhibitor\* of \*SHIP\* function is assessed from the response of the indicator; (4) screening (M2) a substance suspected of \*inhibiting\* \*SHIP\* function, involves allowing \*SHIP\* to react with a \*SHIP\* substrate in the presence of the substance, and taking a first measurement of signal that indicates the extent of the \*SHIP\*/substrate reaction; allowing \*SHIP\* to react with a \*SHIP\* substrate in the absence the substance; and taking a second measurement of the same signal that indicates the extent of the \*SHIP\*/substrate reaction; and comparing the first and second measurements, whereby a substance that \*inhibits\* \*SHIP\* function is selected; (5) a mouse cell (II) comprising a SHIPflox allele of a \*SHIP\* gene which includes a first exon and a promoter, where at least the first exon and the promoter have been deleted in the SHIPflox allele...

... mouse (V) derived from (IV). BIOTECHNOLOGY - Preferred Substance: (I) used in the method comprises a genetic construct that directs expression of an antagonist of a \*SHIP\* function. Preferably the genetic construct comprises an anti-sense polynucleotide, a polynucleotide that bind to \*SHIP\* mRNA, a nucleic acid that hybridizes to a \*SHIP\* mRNA, a recombinant retroviral vector, a ribozyme, an RNA aptamer, a peptidomimetic \*inhibitor\* of \*SHIP\* function, or their combination. Optionally (I) is the small molecule \*inhibitor\* of \*SHIP\* activity having a molecular weight of less than about 10000. Preferred Methods: In (M1), the substance is contacted with a natural killer (NK) cell line, and the response of the indicator (fluorogenic substrate of \*SHIP\*) to the substance is measured by flow cytometry or by a multi-well fluorescence detector. The indicator indicates Ly49 receptors, KIR, Fas, Fas ligand, or phosphatidyl serine in the extracellular leaflet of the plasma membrane. The substance which is contacted with the cell line is a small molecular \*inhibitor\* of \*SHIP\* activity, an anti-sense oligonucleotides, a peptidomimetic \*inhibitor\* of \*SHIP\* function, ribozymes, nucleic acid, polynucleotide, naked DNA, recombinant retroviral vector, RNA aptamer, anti-sense oligonucleotide, or their combination. Most preferably the small molecular \*inhibitor\* is a suicide substrate for \*SHIP\*. In (M2), \*SHIP\* is allowed to react with a \*SHIP\* substrate such as Shc, Grb2, the FcRIIB receptor, PIP3, and IP4, or their modification, in the presence of a substance such as small molecule \*inhibitor\* of \*SHIP\* activity, an oligonucleotide, a peptidomimetic \*inhibitor\* of \*SHIP\* activity, an oligonucleotide, a peptidomimetic \*inhibitor\* of \*SHIP\* function, a ribozymes, a polynucleotide, a polypeptide, an anti-\*SHIP\* antibody, or an RNA aptamer. Preferred Cell: (II) (preferably an embryonic stem cell) is homozygous with regard to the SHIPflox allele. Preferred Transgenic Mouse: (III) has a genotype of \*SHIP\*. (V) does not express \*SHIP\* protein. ACTIVITY - Immunosuppressive. No supporting data provided. MECHANISM OF ACTION - \*SHIP\* function \*inhibitor\*; suppressor of natural killer (NK) cell-mediator activities; antisense

therapy. A cohort of \*SHIP\*<sup>-/-</sup> mice and their \*SHIP\*<sup>+/-</sup> littermates were transplanted with whole bone marrow (BM) from BALB/C mice following lethal irradiation. Mice received 950 Rads prior to BM transplant. Fluorescence activated...

... vs. host re-population for B cells (B220+), myelo-granulocytic cells (Mac-1+/Gr-1+) or T cells (CD3+) in peripheral blood of a representative \*SHIP\*<sup>-/-</sup> BM transplantation survivor. 86% of the \*SHIP\*<sup>-/-</sup> mice survived lethal irradiation without developing GVHD out to 10 weeks post-transplant while only 36% survived in the \*SHIP\*<sup>+/-</sup> cohort. Analysis of the survival differences between the two cohorts using the Kaplan-Meier log-rank test confirmed that survival of \*SHIP\*<sup>-/-</sup> mice was dramatically enhanced relative to their \*SHIP\*<sup>+/-</sup> littermates ( $p=0.007$ ). Nine of fourteen \*SHIP\*<sup>+/-</sup> mice died during the 10 week post-transplant period and prior to death exhibited one or more signs of severe GVHD up to 10 weeks post-transplant. USE - (I) is used in suppressing or preventing \*rejection\* of transplant e.g. bone marrow \*allograft\*, a solid organ \*allograft\* or xenotransplant, or an major histocompatibility complex (MHC) disparate marrow graft having MHC disparity of 1,2,3 or more allelic mismatches, in a patient having a disease such as cancer, autoimmune disease, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). The method is also useful for suppressing or preventing \*rejection\* of a transplant in a patient who is in need of histo-incompatible organ transplant, where the method further involves the step of administering to...

2/3,K/4 (Item 1 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

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137346179 CA: 137(24)346179w PATENT

Control of NK cell function and survival by modulation of SHIP activity

INVENTOR(AUTHOR): Kerr, William G.; Ghansah, Tomar

LOCATION: USA

PATENT: U.S. Pat. Appl. Publ. ; US 20020165192 A1 DATE: 20021107

APPLICATION: US 97101 (20020314) \*US PV233661 (20000919) \*US PV314099  
(20010823) \*US 955174 (20010919)

PAGES: 28 pp., Cont.-in-part of U. S. Ser. No. 955,174. CODEN: USXXCO

LANGUAGE: English CLASS: 514044000; A61K-048/00A; A01K-067/027B

?